New Beginnings
Time to change

Malignant Hyperthermia
2014

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Case History 1
(Firstenberg et al 2010)

A 69 year old man presented for Coronary Artery Bypass Grafting (CABG) with a history of:
- non-insulin dependant diabetes
- severe coronary artery disease
- no previous anaesthetic exposures
- no family history
Case History 1
(Firstenberg et al 2010)

- Induction with Fentanyl, Lignocaine & Propofol, Vecuronium
- Maintenance with Isoflurane & Fentanyl infusion
- Heart was arrested with cold antegrade & retrograde blood cardioplegia
- Patient temperature was maintained at 34°C
Case History 1
(Firstenberg et al 2010)

- 4 vessel CABG was performed
- Routine arterial blood gases were taken
- Isoflurane was distilled into the bypass circuit
- Total Isoflurane time was 4.5 hours
Case History 1
(Firstenberg et al 2010)

- On arrival to Intensive Care Unit the patient developed a tachycardia & became hyperthermic
- A chest x-ray was normal
- Haemodynamics were controlled by nicardipine infusion & fentanyl
- Arterial Blood gases revealed severe respiratory acidosis – minute volume was adjusted
Case History 1
(Firstenberg et al 2010)

- Follow-up gases showed increasing CO2 levels
- Hyperkalemia
- Temperature was increasing
- Musculoskeletal stiffness was noted
- Masseter rigidity
- Malignant Hyperthermia was finally suspected
Malignant Hyperthermia remains an important risk for general anaesthesia patients (Metterlein et al. 2011)
Malignant Hyperthermia

This occurs in genetically predisposed humans

Malignant Hyperpyrexia is a synonymous term
Malignant Hyperthermia

Definition: A catastrophic, often fatal syndrome triggered by:

Anaesthetic Triggers
- Inhalational agents
- Depolarizing muscle relaxants
- Rocuronium - 2 cases where Rocuronium was the most likely trigger agent (Aston et al. 2012)
- Incidence 1:3,000 to 1:50,000 anaesthetics (Hirshey Dirksen et al. 2012)
Malignant Hyperthermia

Non Anaesthetic Triggers

- Certain myopathies (i.e., Evans, King Denborough)
- Emotional stress
- Heat stroke
- Neuroleptic malignant syndrome
- Strenuous exercise
- Trauma
Excessive amounts of calcium are released from the sarcoplasmic reticulum in skeletal muscle.

- Calcium $\rightarrow$ contraction $\rightarrow$ heat
- $O_2$ consumption $\rightarrow$ $CO_2$ $\rightarrow$ calcium $\rightarrow$ contraction $\rightarrow$ acid $\rightarrow$ heat
Ryanodine is a large protein molecule. It covers the opening on the sarcoplasmic reticulum. Ryanodine regulates calcium release. The majority of Malignant Hyperthermia susceptibility individuals have a defect in the ryanodine receptor type 1 (RYR1) gene.

(Hirshey Dirksen et al 2012)
More than 80 genetic defects have been linked to Malignant Hyperthermia (MH)

Susceptibility is an autosomal dominant inherited disorder of skeletal muscle

A child or sibling of a susceptible patient has a 50% chance of inheriting a defective gene

(Mitchel-Brown 2012)
Recent research looked at 24 cases of MH in cardio-thoracic patients:
- In 14 cases MH occurred during or shortly after bypass.
- Dantrolene was used in all but 1 case where the patient died.
- All other patients who received Dantrolene survived.

(Metterlein et al. 2011)
Research tells us...

  - 286 cases studied
  - Young males 74.8%
  - 6.5% had a family history
- ‘77 of 152 patients reported 2 previous unremarkable anaesthetics’ (Larach et al 2010)
- 50% of cases had had previous anaesthesia (Blinn 1995)
Research tells us….

- In 10 cases skin liquid crystal temperature probes did not trend ↑ temp
- Accurate temperature monitoring during general anaesthesia and early Dantrolene administration may decrease MH mortality by 35%
- 21 experienced haematological / neurological complications with a temp less than 41.6 (human critical thermal maximum) (Larach et al 2010)
12 Anaesthetics and triggered fatally on the 13th (Blinn 1995)

MH is most likely to occur in the operating theatre (Hommertzheim 2006)

It can also present in the PACU and possibly up to 12 hours post-operatively (Hommertzheim 2006)

Suspected case using Deflurane only presented 6 hours post-operatively (Papadimos 2004)
TRIGGER AGENTS

Volatile Inhalational agent
- Isoflurane
- Sevoflurane
- Desflurane
- Halothane
- Enflurane
- Ether, Cyclopropane

Depolarizing muscle relaxants
- Suxamethonium Chloride
Safe Agents

**Intravenous agents**
- Propofol
- Barbiturates
- Benzodiazepines
- Opiates

**Muscle relaxants**
- Non-depolarizing (?????? Rocuronium)

**Inhalation agents**
- Nitrous oxide

**Local anaesthesia** - Amides / esters
SIGNS OF MALIGNANT HYPERTHERMIA

Early (s+s may be seen in any order)
- Tachycardia
- Tachypnoea
- Sweating
- Sudden rise in end – tidal CO₂
- Temperature
- Ventricular extra systole
- Unstable B/P
- Rigidity (immediately after sux)
- Masseter muscle rigidity
Research showed frequent early signs were:

- Hypercarbia
- Sinus tachycardia
- Masseter spasm
- In 63.5% temp was the 1st to 3rd sign

(Larach et al 2010)
SIGNS OF MALIGNANT HYPERTHERMIA

Late
- Cyanosis
- Skin mottling
- Hyperkalemia
- Myoglobinuria
- Elevated Creatine Kinase
TREATMENT

- Stop trigger agents immediately
- Change anaesthetic machine/circuit
- Change catheter mount (if old black liquorice stick)
- Stop or expedite surgery
- Administer 100% oxygen – hyperventilate
- Call for help – press emergency bell
- Obtain malignant hyperthermia kit
- Administer Dantrolene 2.5mg/kg up to 10mg/kg
TREATMENT

- Notify nursing supervisor & pharmacy department
- Send orderly for buckets of ice
- Cool patients and monitor temperature
- Ice to axilla and groin
- Cool I.V. fluids
- Cooling blanket (Polar Bear)
- Assist in line insertion
- Central line
- Arterial line
ASSIST IN TREATMENT OF:

- Arrhythmia’s
- Electrolyte imbalance
- Maintenance of cardiac function
- Urinary catheterisation
  - Careful observation of output and colour of urine
DANTROLENE SODIUM
(Dantrium)

- Dantrium is a skeletal muscle relaxant
- Decreases the amount of calcium released by the sarcoplasmic reticulum
- Reverses the pathophysiology of Malignant Hyperthermia
- Case fatality rate has fallen from 70% in the 1970’s to less than 10% in 2006
- Preparation: 20mg vials – powder to be mixed with 60mLs sterile water
- Sterile warm water or room temperature
- Sodium Hydroxide and 3g Mannitol
DANTROLENE SODIUM (Dantrium)

- Initial dose 2.5mg x 70kg = 175mg = 9 vials
- 10mg x 70kg = 700mg = 35 vials
- The median dose of Dantrolene was 5.9mg/kg (Larach et al., 2010)
DANTROLENE SODIUM (Dantrium)

- Subsequent doses may be required over the coming hours or days - 1mg/kg 6 hourly for the first 24-48 hours (Carter – Templeton 2006)
- MH symptoms re-occur in 25% of patients after episode if there is no further Dantrolene (Mitchel-Brown 2012)
- pH 9.5 – care must be taken to; prevent extravasation, be watchful for thrombophlebitis
- Solution must be protected from light and used within 6 hours
Dantrium® Intravenous
(dantrolene sodium for injection)

For treatment of malignant hyperthermia
For intravenous use only.

CAUTION: Federal law prohibits dispensing without prescription.

Procter & Gamble
PHARMACEUTICALS
Dantrolene Pfizer has releasing a new formulation of Dantrolene (Dantrium IVTM) in Australasia late this year.

After more than 20 years of concern about the difficulties of emergency preparation of this drug, improvements in the lyophilisation (freeze-drying).

There are no changes to:
- dose per vial (20mg)
“New”

- diluent (60 mL sterile water for injection)
- dose (2.5mg/ kg increments regardless of age, with no upper dose limit)
- “Old” formulation dantrolene will be replaced with Dantrium IVTM as stock expires

(Australian & New Zealand College of Anaesthetists 2011)
Testing

Caffeine Halothane Contractility test
- Very sensitive and detects virtually all patients with MH
- Costly
- Requires fresh muscle biopsy

Molecular genetic diagnostic test
- Blood sample
- DNA testing
- Not all patients with MH have DNA change
- Test will only detect 30% of sufferers
Dantrolene stocks:

- ‘The MHANZ group recommends that a minimum of 24 (20mg) vials of Dantrolene are held in any anaesthetising location where triggering anaesthesia is performed. Larger or remote hospitals should carry 36 vials.

- This stock level represents 2-3 x 2.5mg/kg doses for an average sized adult and is a reasonable compromise between clinical need and economy.

- Dantrolene cost is approximately AUD $900 and NZD $1600 for 12 ampoules’.

(ANZCA Guidelines January 2007)
Take home message…

New Beginnings Time to Change….
Educate our colleagues outside the operating suite
References

References


References